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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,987	03/05/2002	Robert B. Dickson	P 0280712 DIRO421009	4488
909	7590	08/16/2006	EXAMINER	
PILLSBURY WINTHROP SHAW PITTMAN, LLP P.O. BOX 10500 MCLEAN, VA 22102			UNGAR, SUSAN NMN	
			ART UNIT	PAPER NUMBER
			1642	
DATE MAILED: 08/16/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/087,987

Applicant(s)

DICKSON ET AL.

Examiner

Susan Ungar

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 05 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 34,35,39,41-44,48 and 49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 34-35, 39, 41-44, 48-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/5/06th.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: _____.

1. The Amendment filed June 5, 2006 in response to the Office Action of January 4, 2006 is acknowledged and has been entered. Previously pending claims 37, 38, 40, 50 have been canceled and claims 34-36, 41, 42, 49 have been amended. Claims 34-36, 39, 41-44 and 48-49 are currently being examined.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The following rejections are being maintained:

Claim Rejections - 35 USC 112

4. Claims Claims 34-36, 39, 41-44 and 48-49 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed January 4, 2005, Section 5, pages 7-12.

Applicant argues that the language in the specification drawn to the frequent reiteration of statements in the specification indicating that at the time the invention was made, it was unknown if the claimed invention would function as claimed was merely the conscientious indication by medical scientists that indicated that further experimentation is needed across the range of subject matter that was investigated in support of the invention. The argument has been considered but has not been found persuasive because despite the data presented, Applicant consistently uses phrases such as “within a breast tumor, such activity (matriptase) may contribute to the tumorigenic and metastatic properties of breast cancer cells”, “if the catalytic activity of the serine protease matriptase is important for growth and/or invasion of breast cancer cells in human breast tumors” clearly indicating that at the time the invention was done, additional work was required in order to determine if the claimed invention was enabled.

Applicant argues that the specification provides data that demonstrates that maltriptase is consistently and efficiently expressed by tumors and that matriptase expression by malignant cancer cells is constitutive whereas matriptase expression in normal tissue is sensitive to regulatory factors in serum and points to paragraph 95. The argument has been considered but has not been found persuasive because a review of the specification reveals that the specification as originally filed does not comprise a paragraph 95. Further, although the data demonstrates that maltriptase is expressed by tumors, this information, does not enable the claimed invention for the reasons of record.

Applicant argues that the information drawn to expression in tumors is useful for diagnosis. The argument has been considered but has not been found persuasive because applicant is arguing limitations not recited in the examined claims as currently constituted.

Applicant argues that submitted post-filing references corroborate the teachings of the specification and demonstrate that inhibition of the expression of matriptase in vivo in nude mice inhibits the growth of tumors and points to Suzuki et al, in particular page 14906 as well as List et al and Kang et al. The argument has been considered but has not been found persuasive because a review of List et al, reveals that the model used to collect the data is not commensurate in scope with the claimed invention. In the model used, transgenic mice were produced that constitutively express matriptase wherein it was found that the mice developed spontaneous squamous cell carcinomas. However, it is not clear from the reference whether or not control mice were found to spontaneously develop squamous cell carcinomas. Since it would be expected that control mice would express both matriptase and its cognate inhibitor HAI-1, given that it appears that

control mice would not develop the spontaneous tumors, it is not clear how the finding of spontaneously developed tumors in transgenic mice that constitutively express matriptase construct is relevant to the enablement of the claims, given the issue raised previously drawn to endogenous inhibitors and the reasonable expectation that matriptase would be inhibited, even in the absence of administered inhibitors. Further, the List reference goes on to demonstrate that production of transgenic mice that constitutively express both matriptase and HAI-1 led to the complete negation of both tumor susceptibility and all premalignant manifestations of matriptase overexpression (see p. 1942, second column), supporting Examiner's argument. Even if it were to be found that inhibiting matriptase could treat cancer associated with reduced expression of HAI-1, the claims would still not be enabled because the claims are specifically drawn to determining only whether or not matriptase is activated and in the absence of a requirement to identify HAI-1 expression as well, one would not know how to predictably identify distinguish between those patients that could be successfully treated and those that could not. The specification clearly teaches that "there remains a need for the elucidation of the mechanisms through which the CEA (*sic*) plays a role in cancer and the design of therapeutic and diagnosis protocols based on the elucidation of those mechanisms". It is clear, that the claims as currently constituted do not take into account a HAI-1 dependent mechanism and at the time the invention was made, although Applicant hypothesized that such a mechanism might exist, it is clear from the specification as originally filed that at the time the invention was made, this mechanism was unknown.

Further, a review of Suzuki et al, page 14906 reveals that the reference is once again not commensurate in scope with the claimed invention. The data is

drawn to the survival of tumor bearing mice, wherein the mice were injected with ovarian cancer cells that had been transfected with matriptase antisense wherein the survival time of the mice with cells transfected with matriptase antisense was significantly longer than those not transfected. However, no information drawn to extent of HAI-1 expression is presented in the reference and thus it is not possible to determine from the information in the reference whether or not the cancer cells are deficient in HAI-1 and given the information in the List et al reference, in the absence of further information, the Suzuki et al reference cannot be evaluated.

A review of the Kang reference reveals that the reference is drawn to *in vitro* Tissue Microarray Analysis which revealed that high-level expression of matriptase, and HAI-I were associated with poor patient outcome. However, this reference does not support the claimed invention because it would be expected, given the high level of expression of matriptase and HAI-1, that the effects of the high expression of HAI-I would cancel out any putative effects of matriptase on tumor, as demonstrated by LIST et al and supports Examiner's finding of a lack of enablement for the claimed invention.

Applicant admits on the record that treatment of cancer is unpredictable, but that despite that unpredictability one would be able to practice the claimed invention without having to perform undue experimentation and argues that the teachings of Gura are not appropriate since Gura refers to successful compounds that have been approved by the FDA which is a standard not appropriate to patent prosecution and argues that the Curti, Hartwell, White, Jain references are not relevant. The argument has been considered but has not been found persuasive given that Applicant admits on the record that treatment of cancer is unpredictable

and given that neither the art of record nor the specification as originally filed enables the claimed invention for the reasons of record.

Applicant further argues that Suzuki et al enables the claimed invention and that Foltz et al and Galkin et al similarly enable the claimed invention. However, a review of Foltz et al reveals that only the abstract was submitted so that the information in the reference cannot be evaluated. Further, a review of Galkin et al reveals that only the abstract was submitted so that the information in the reference cannot be evaluated.

Applicant argues that agents that block the activity of active matriptase were described prior to the filing of the present application. The argument has been considered but does not enable the claimed invention for the reasons of record.

Applicant's arguments have not been found persuasive and the rejection is maintained.

5. Claim 41 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth set forth in the paper mailed January 4, 2005, Section 7, pages 16-18.

Applicant submits an amendment to the specification as required and submits a Deposit Declaration. However, upon review of the Declaration, it is found that the Declaration is defective because the deposit was made after the filing of the application and Applicant has not submitted a statement, from a person in a position to corroborate the fact, stating that the biological material which is deposited is a biological material specifically identified in the application as filed, see 37 CFR 1.801.

New Grounds of Objection

6. It is noted that a review of the specification has revealed the statement in the specification at paragraph 0006 that “Thus, there remains a need for the elucidation of the mechanisms through which the CEA plays a role in cancer and the design of therapeutic and diagnosis protocols based on the elucidation of those mechanisms.” Since the specification is not drawn to CEA, it appears that the recitation of CEA is an inadvertent typographical error. Appropriate correction is required.

New Grounds of Rejection

7. Claim 49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 49 is rejected under 35 USC 112, second paragraph because the claim recites the phrase “the method of claim 34, wherein the antibody that blocks the activity of active matriptase binds specifically to and directly blocks the activity of activated matriptase.” However there is no antecedent basis for an antibody that blocks the activity of activated matriptase in claim 34 from which claim 49 depends.

9. No claims allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

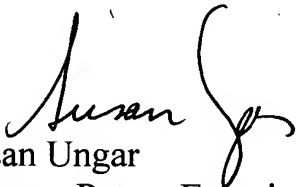
A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE

ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
August 9, 2006